

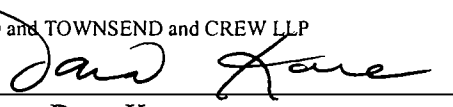
I hereby certify that this correspondence is being filed in the U.S. Patent and Trademark Office via EFS on November 27, 2007.

PATENT

Attorney Docket No.: 016325-013900US

TOWNSEND and TOWNSEND and CREW LLP

By: \_\_\_\_\_



Dana Kane

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of:

Allan BERNARD et al.

Application No.: 10/516,635

Filed: November 30, 2004

For: METHODS OF DIAGNOSING &  
TREATING DIABETES AND INSULIN  
RESISTANCE

Customer No.: 20350

Confirmation No. 2823

Examiner: Gyan Chandra

Technology Center/Art Unit: 1646

AMENDMENT

Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

In response to the Office Action mailed July 27, 2007, please enter the following amendments and remarks. A petition for a one-month extension of time, from October 27, 2007 through November 27, 2007, accompanies this Amendment. An information disclosure statement (IDS) also accompanies this Amendment.

**Amendments to the Specification** begin on page 2 of this paper.

**Amendments to the Claims** are reflected in the listing of claims which begins on page 3 of this paper.

**Remarks/Arguments** begin on page 5 of this paper.

**Amendments to the Specification:**

Please replace paragraph [049] with the following amended paragraph:

--[049] Two examples of algorithms that are suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0 algorithms, which are described in Altschul *et al.* (1977) *Nuc. Acids Res.* 25:3389-3402, and Altschul *et al.* (1990) *J. Mol. Biol.* 215:403-410, respectively. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information (<http://www.ncbi.nlm.nih.gov/>). This algorithm involves first identifying high scoring sequence pairs (HSPs) by identifying short words of length W in the query sequence, which either match or satisfy some positive-valued threshold score T when aligned with a word of the same length in a database sequence. T is referred to as the neighborhood word score threshold (Altschul *et al.*, *supra*). These initial neighborhood word hits act as seeds for initiating searches to find longer HSPs containing them. The word hits are extended in both directions along each sequence for as far as the cumulative alignment score can be increased. Cumulative scores are calculated using, for nucleotide sequences, the parameters M (reward score for a pair of matching residues; always > 0) and N (penalty score for mismatching residues; always < 0). For amino acid sequences, a scoring matrix is used to calculate the cumulative score. Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T, and X determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences) uses as defaults a wordlength (W) of 11, an expectation (E) or 10, M=5, N=-4 and a comparison of both strands. For amino acid sequences, the BLASTP program uses as defaults a wordlength of 3, and expectation (E) of 10, and the BLOSUM62 scoring matrix (*see* Henikoff and Henikoff (1989) *Proc. Natl. Acad. Sci. USA* 89:10915) alignments (B) of 50, expectation (E) of 10, M=5, N=-4, and a comparison of both strands.--